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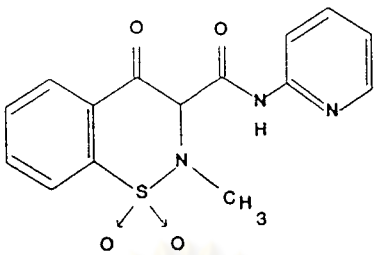
APPENDICES

Appendix I

Details of Some Excipients.

Piroxicam



The molecular structure of piroxicam is shown above. The empirical formula is C_{15} H_{13} N_3 O_4 S with a molecular weight of 331.35. The chemical name is 4-hydroxy-2-methyl-N-2-pyridyl-2H-1, 2-benzothiazine-3-carboxamide-1, 1-dioxide.

Piroxicam is one of the non-steroidal anti-inflammatory drugs (NSAIDS). It was first developed by Pfizer and entered into medical praxis in 1970 (Mihalic et al., 1986). Piroxicam is an odorless, colorless crystalline powder with a bitter taste. It is not soluble in water and cyclohexane, sparingly soluble in diisopropyl ether and toluene, and only slightly more soluble in lower aliphatic alcohols. It is soluble in some polar organic solvents such as dimethylformamide (1 g./10 ml.), dimethylsulfoxide (1 g./10 ml.), chloroform (1 g./20 ml.), and somewhat less soluble in dioxane (1 g./40 ml), acetone (1 g./50 ml.) and ethyl acetate (1 g./80 ml.). Solubility of piroxicam increases with increasing pH (Tsai, 1985). Piroxicam has pKa's of 1.8 and 5.1.

Storing of piroxicam in a brown powder glass in the dark at 20°C and 40°C for two years showed no changes in color, smell, taste and shape of crystals. The degradation product could not be detected by TLC and HPLC.

Irradiation of piroxicam stored in colorless bottles for 72 hours at the wavelength of 300-380 mm. at 30 ± 0.5°C showed a good photostability.

Acute toxicity of piroxicam is low : the LD_{50} for orally applied piroxicam is 360 mg./kg. in the mouse, 270 mg./kg. in the rat and over 700 mg./kg. in the dog. When it was administered intraperitonially, the LD_{50} values are 360 and 220 mg./kg. in the mouse and rat, respectively.

Piroxicam is effective on anti-inflammatory, antipyretic and analgesic action. The attribution of their usage are in the cases of rheumatoid arthritis and osteoarthritis. The mode of action of piroxicam is not fully understood, but the mechanism of its activity may exist in its ability to inhibit the activity of enzyme cyclo-oxygenase which results in the decrease in formation of precursors of prostaglandins and thromboxanes from arachidonic acid.

In a comparative study (Schiantrarelli and Cadel, 1981), it was observed that the anti-inflammatory activity of piroxicam (Feldene®) on carragenin edema in rats was equal when it was administered orally and rectally. It was twice as effective as an indole derivative (Indocin®) and 20 times as effective as phenylbutazone (Butazolidin®). Being an analgesic, piroxicam is more potent than aspirin, fenoprofen (Nalfon®), ibuprofen (Motrin®), arylacetic derivative (Naprosyn®) and phenylbutazone (Butazolidin®).

Piroxicam is readily absorbed after oral or rectal administration. Peak plasma concentrations are attained about 2 hours after a single oral dose and about 5.5 hours after a rectal administration using suppositories. It is accumulated after repeated doses to reach steady-state in about seven days. The drug is extensively metabolised to apparently inactive metabolites and has a half-life of about 40 hours in man. Due to the extended plasma half-life of piroxicam, plasma concentrations remain very stable over the next 24-48 hours. Mean peak plasma concentrations are roughly related to dosages, being 0.85 mcg./ml. and 13.5 mcg./ml. after a single 10 or 100 mg. dose, respectively. A single dose of 20 mg. will generally produce a peak plasma concentration of 1.5 to 2.0 mcg./ml. while a maximum plasma level after repeated doses may stabilize at about 3.8 mcg./ml.

Although the usual oral dose of 20 mg. of piroxicam is well torelated by the patients, several side effects have been reported including : gastrointestinal disturbances, edema, dizziness, headache and skin rash, etc. In addition, peptic ulcer has been reported in about 9 % of the patients with chronic arthritis when they were treated with 20 mg. of daily oral dose (Pisko et al., 1980). Because several side effects are caused by the oral use of piroxicam, the development of various topical dosage forms of the drug has been proposed.

The topical anti-inflammatory effects of percutaneous piroxicam from an ointment have been studied by some researchers (Larson and Lombardino, 1980; Schiantarelli et al., 1982). Topically applied piroxicam has been shown to have activity comparable with that of the equal orally administered dose when it was applied the day before or 15 days after adjuvant induced arthritis, indicating that the topical piroxicam is responsible for the anti-inflammatory activity (Larson and Lombardino, 1980).

Piroxicam release and percutaneous absorption from dermatological bases have been studied (Tsai, 1985; Dallas, 1987; Babar et al., 1990). Babar et al., 1990 demonstrated that a general rank order for the in-vitro drug release from all the bases evaluated was : gel base > hydrophilic base > emulsion base.

Poloxamer 407 (Pluronic F-127®)

Pluronic F-127 is one of the series of poly $(oxyethylene)_x$ - poly $(oxypropylene)_y$ block copolymer. Its empirical formula is shown below,

$$HO - (CH_2 - CH_2O)_x - (CH_2 - \underset{CH_3}{CH} - O)_y - (CH_2 - CH_2 O)_x - OH$$

where x is 98 and y is 67, and the average molecular weight is 12,500. Pluronic is a white, waxy, free-flowing prilled granules or cast solid. It is practically tasteless and odorless. Pluronic F-127 is soluble in water and mixtures of alcohol and water. It is insoluble in ether, paraffin waxes and fatty oils. It is more soluble in cold water than in hot water due to the increase in solvation and hydrogen bonding at lower temperature. Aqueous solutions of between 20 and 30 % w/w pluronic F-127 have the interesting characteristic of reverse thermal gelation, that is, they are liquid at refrigerated temperature (4-5°C) but gel upon warming to ambient levels (Schmolka, 1972). The gelation is reversible upon cooling.

The viscosity of pluronic F-127 gels is affected by electrolytes, humectants, alcohols and surfactants. For example, the gel-formation temperature is depressed by sodium chloride and raised by ethanol. The gels are incompatible with anionic surfactants and are adversely affected by low pH values.

Pluronic F-127 is used as thickening agent and gelling agent in pharmaceutical and cosmetic preparations.

Carbopol

Carbopol, a carboxyvinyl polymer, is probably the most outstanding gum-like materials used in pharmaceutics and cosmetics. The empirical formula is demonstrated below,

$$(C_3 H_4 O_2)_x (-C_3 H_5 - Sucrose)_y$$

with different molecular weight. Carbopol is a white, fluffy, acidic, hygroscopic powder with a slight characteristic odor. Carbopol is soluble in water, alcohol, and glycerin.

It is usually sold in the acid form, although two ammonium salts are now available. Table 11 shows the differences in properties of the five types.

Table 11 : Properties of five different types of carbopol.

Number	Chemical form	Viscosity	Neutralized clarity	Yield value	Effect of temp.on vis.
934	Acid form	High	Good	Lowest	Second best
940	Acid form	High	Best	Next best	Best
941	Acid form	Lower	Good	Best	Poorest
960	Ammonium Salt 934	High	Fair	-	-
961	Ammonium Salt 941	Lower	Fair	-	-

Since carbopol is generally bought in the acid form which the pH of a 1 % dispersion of carbopol in water is approximately 3.0, it must be neutralized when it is used. Various alkalies are used for specific purposes. Some of the neutralizing ratios are given in Table 12. It shows the amounts of respective alkalies required to bring 1 part carbopol, either type, to a pH of approximately 7.0.

Table 12 : The amounts of various alkalies required to neutralized 1 % carbopol.

Alkalies	%
Ammonia (28 %)	0.70
Sodium carbonate	0.72
Borax (hydrated)	1.39
Monoethanolamine	0.68
Triethanolamine	1.35
Diisopropanolamine	1.70
Sodium hydroxide	0.40
Di - (2-ethyl hexyl) amine	3.20
Ethomeen C 25	11.50
Armeen CD	2.70

In a system that can tolerate sodium hydroxide when it was used as a neutralizer, it produces the clearest, thickest and least sticky gel all the way around. However, some of these characteristics are subjective. If sodium hydroxide could not be used as the neutralizer, triethanolamine would be the neutralizer of choice.

Neutralized aqueous gels of carbopol are more viscous between pH 6 and pH 11. The viscosity is considerably reduced if the pH is < 3 or > 12. The viscosity is also reduced in the presence of strong electrolytes. Gels lose viscosity rapidly on exposure to sunlight, but this reaction can be minimized by the addition of an antioxidant.

Carbopol is more commonly used in pharmaceutical liquid and semi-solid dosage forms than in tablets. Carbopol is used as emulsifying agent (0.1-0.5 %), suspending agent (0.5-1.0 %), and gelling agent (0.5-2.0 %) in pharmaceutical and cosmetic preparations. Its wide usefulness is complimented by the lubricity it imparts to the product.

Hydroxypropyl Methylcellulose (HPMC)

Hydroxypropyl methylcellulose is a cellulose hydroxypropyl methyl ether. The empirical formula is shown below,

$$C_8 H_{15} O_6 - (C_{10} H_8 O_6)_n - C_8 H_{15} O_5$$

with an approximate molecular weight about 86,000. Hydroxypropyl methylcellulose is an odorless, tasteless, white or creamy-white fibrous or granular powder. It is soluble in cold water, forming a viscous colloidal solution; insoluble in alcohol, ether and chloroform; but soluble in mixtures of methyl alcohol and methylene chloride. It is available in two viscosity ranges, 50 and 4,000 cps. It undergoes a reversible transformation from sol to gel upon heating and cooling, respectively. Solutions of hydroxypropyl methylcellulose are stable at pH 3.0 - 11.0. It is incompatible with extreme pH conditions and oxidizing materials.

To prepare an aqueous solution, it is recommended to disperse and thoroughly hydrate hydroxypropyl methylcellulose in about 1/5 to 1/3 of the required amount of water at 80-90°C and add cold water or ice while it is stirring vigorously. Then add cold water to volume.

Hydroxypropyl methylcellulose is used as film former, binder, thickener, emulsifier, stabilizer, suspending agent and gelling agent in pharmaceutical preparations.

Hydroxyethyl Cellulose (HEC)

Hydroxyethyl cellulose is a cellulose hydroxyethyl ether. The empirical formula is shown below,

$$(C_{12}\,H_{21.5}\,O_8)_n$$

with a wide variety of molecular weight. Cellosize and Natrosol are two trade names for hydroxyethyl cellulose. A wide range of viscosity type is available. Hydroxyethyl cellulose is a light tan or cream to white powder. It is odorless and tasteless. Hydroxyethyl cellulose dissolves in water, either cold or hot, to form clear, smooth, uniform solutions. As normally substituted, hydroxyethyl cellulose is insoluble in most organic solvents. In a few of the polar solvents, such as the glycols, it either swell or is partially soluble.

In preparing solutions of hydroxyethyl cellulose, the dry loose material is sifted into water at 65°C, while agitating continuously. A slower method is to mix the powdered hydroxyethyl cellulose with six to eight parts of water, producing a thick slurry, and to agitate vigorously a few minutes. Allow to set overnight in a refrigerator, then add water to volume.

Variations in pH between about 2 and 12 have little effect on the viscosity of solutions. Hydroxyethyl cellulose is subject to enzymatic degradation, consequent loss of viscosity of its solutions. Hydroxyethyl cellulose solutions tolerate salts except sulfates and especially aluminium salts. Strong acids and alkalies are undesirable. Solutions of hydroxyethyl cellulose can tolerate 10 to 15 % of alcohols or acetone.

It is used pharmaceutically as a thickening agent, protective colloid, binder, stabilizer, suspending and gelling agent. The concentration to be used is dependent on the solvent and molecular weight of the grade used.

Appendix II

Data of Piroxicam Fluxes from Various Gel Bases through Silastic®.

Gelling Agent : Pluronic F - 127, 20.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4332	0.7149	1.7791	2.8303	3.6224	4.6975

$Y = - 0.1323 + 9.5941 x$

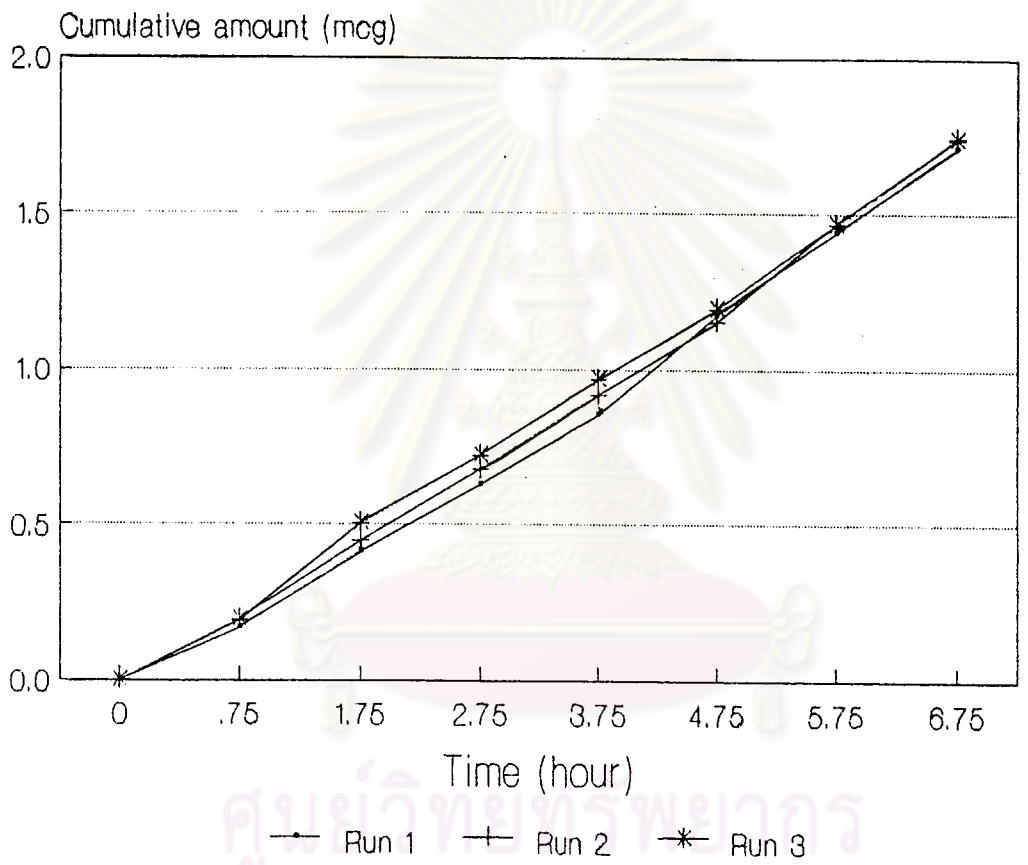
$r^2 = 0.9975$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.1497	0.1664	0.1736	0.1901	0.1946	0.1940
1.75	0.2856	0.2468	0.2851	0.2593	0.3893	0.3095
2.75	0.2168	0.2160	0.2132	0.2246	0.2363	0.2185
3.75	0.2459	0.2230	0.2478	0.2360	0.2847	0.2469
4.75	0.4109	0.3204	0.2595	0.2432	0.2499	0.2265
5.75	0.3186	0.2660	0.3702	0.3123	0.3216	0.2691
6.75	0.3352	0.2756	0.3195	0.2807	0.3359	0.2777
Steady-state slope (mcg/hr)	0.2852		0.2821		0.2589	
Lag time (hr)	0.71		0.58		0.06	
Steady-state flux (mcg/hr. cm^2)	0.1852		0.1832		0.1681	
r^2	0.9983		0.9978		0.9979	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 0.1788 \pm 0.0093 \quad$ % CV = 5.23

Piroxicam flux from pluronic F-127 gel base through silastic®.



Gelling Agent : Carbopol - 940, 1.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4320	0.7826	1.6015	2.3762	3.2223	4.0567

$Y = - 0.0083 + 8.0780 x$

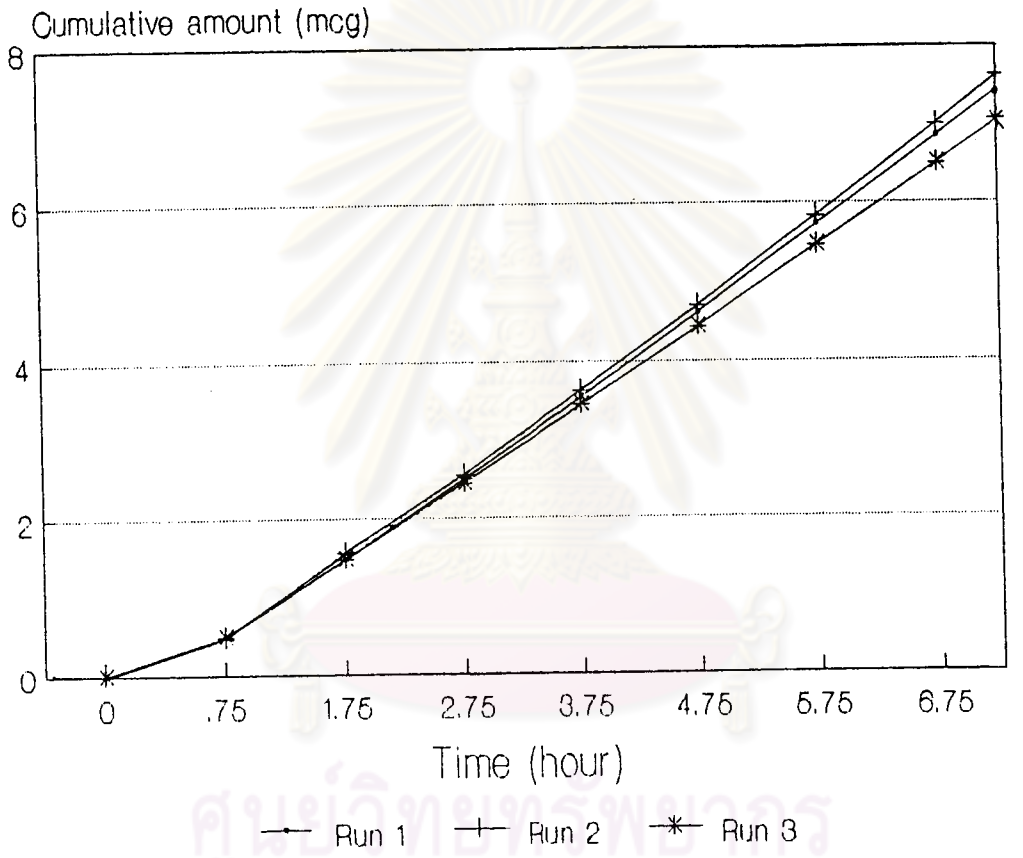
$r^2 = 0.9996$

Diffusion Run Data

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.6864	0.4936	0.6592	0.4675	0.6509	0.4863
1.75	1.3526	0.9672	1.5453	1.0884	1.3442	0.9977
2.75	1.4514	1.0372	1.4136	0.9962	1.2952	0.9619
3.75	1.4508	1.0366	1.5266	1.0754	1.3392	0.9941
4.75	1.5110	1.0797	1.5410	1.0856	1.3452	0.9989
5.75	1.5510	1.1078	1.5989	1.1263	1.3810	1.0251
6.75	1.5552	1.1107	1.6579	1.1676	1.3899	1.0317
7.25	0.7668	0.5505	0.8271	0.5852	0.8383	0.6246
Steady-state slope (mcg/hr)	1.1081		1.1526		1.0624	
Lag time (hr)	0.58		0.67		0.59	
Steady-state flux (mcg/hr. cm^2)	0.7196		0.7484		0.6899	
r^2	0.9999		0.9999		0.9988	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 0.7193 \pm 0.0292 \quad$ % CV = 4.07

Piroxicam flux from carbopol-940 gel base through silastic®.



Gelling Agent : Hydroxypropyl Methylcellulose, 3.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4526	0.8123	1.5349	2.4769	3.0102	4.0126

$Y = 0.0338 + 7.8044\ x$

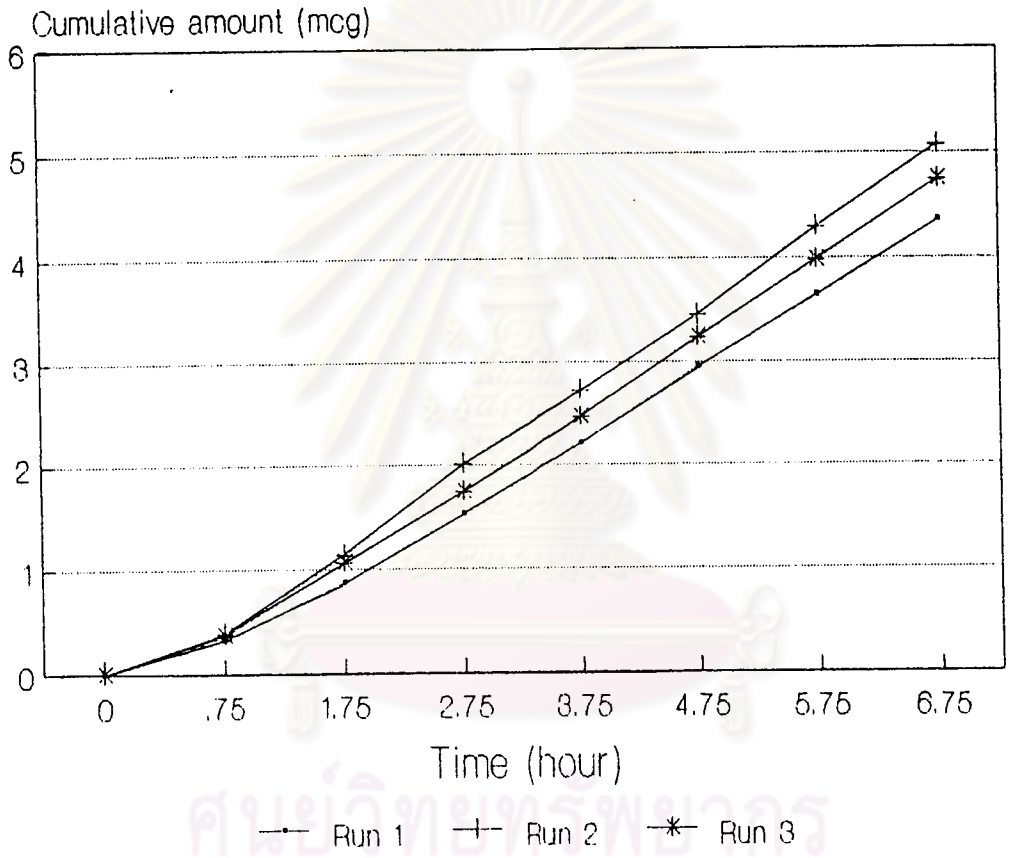
$r^2 = 0.9955$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.4618	0.3146	0.5520	0.3758	0.5039	0.3588
1.75	0.7854	0.5528	1.0754	0.7556	0.9559	0.7045
2.75	0.9285	0.6578	1.2369	0.8728	0.9206	0.6770
3.75	0.9563	0.6785	1.0198	0.7148	0.9805	0.7229
4.75	1.0352	0.7364	1.0382	0.7284	1.0411	0.7694
5.75	0.9821	0.6974	1.2061	0.8501	1.0075	0.7438
6.75	1.0166	0.7227	1.1103	0.7805	1.0468	0.7736
Steady-state slope (mcg/hr)	0.7167		0.7927		0.7604	
Lag time (hr)	0.66		0.35		0.51	
Steady-state flux (mcg/hr. cm^2)	0.4654		0.5147		0.4938	
r^2	0.9999		0.9992		0.9999	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 0.4913 \pm 0.0247 \quad$ % CV = 5.04

Piroxicam flux from HPMC gel base through silastic®.



Gelling Agent : Hydroxyethyl Cellulose, 2.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4526	0.8123	1.5349	2.4769	3.0102	4.0126

$Y = 0.0338 + 7.8044\ x$

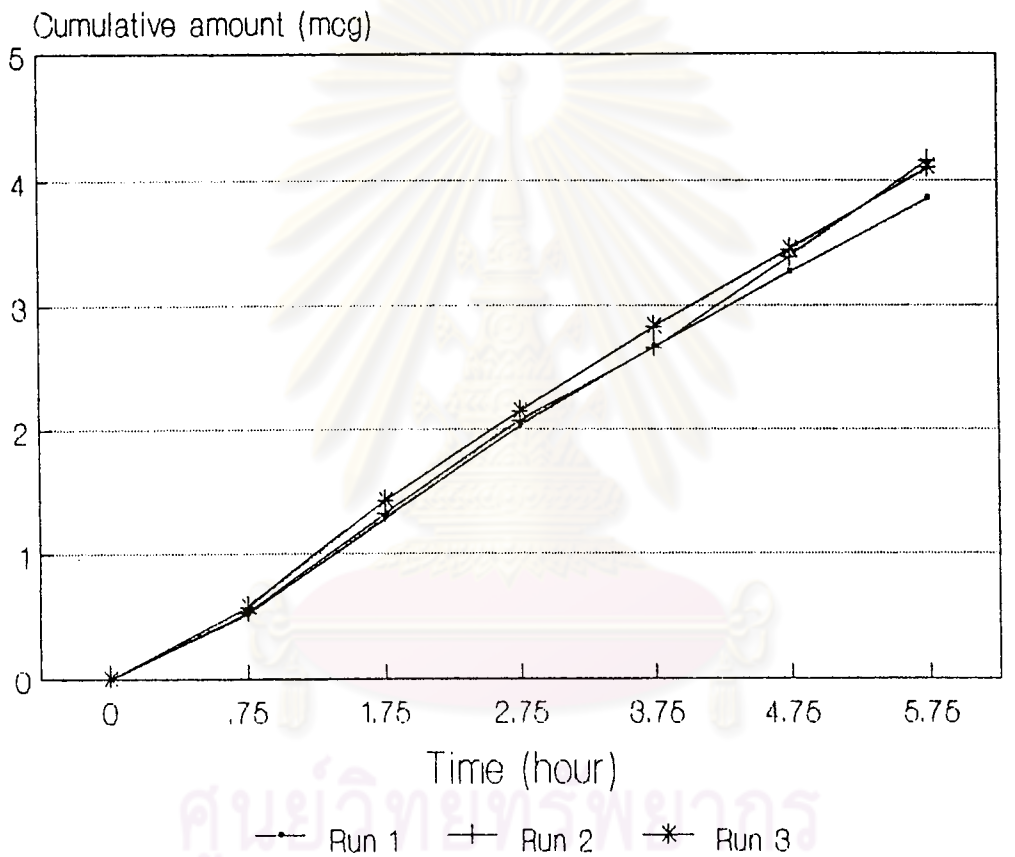
$r^2 = 0.9955$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.7330	0.5143	0.7688	0.5332	0.7814	0.5710
1.75	1.0778	0.7680	1.1142	0.7833	1.1462	0.8493
2.75	1.0386	0.7393	1.0710	0.7522	0.9812	0.7235
3.75	0.9042	0.6440	0.8426	0.5864	0.9348	0.6878
4.75	0.8588	0.6067	1.0490	0.7364	0.8453	0.6198
5.75	0.8206	0.5786	1.0817	0.7601	0.8887	0.6526
Steady-state slope (mcg/hr)	0.6095		0.6985		0.6500	
Lag time (hr)	-0.59		-0.14		-0.57	
Steady-state flux (mcg/hr. cm^2)	0.3958		0.4536		0.4221	
r^2	0.9994		0.9966		0.9996	

* PAR = Peak Area Ratio $\bar{J}ss = 0.4238 \pm 0.0289$ % CV = 6.83

Piroxicam flux from HEC gel base through silastic®.



Appendix III

Data of Piroxicam Fluxes from Various Gel Bases through Pig Skin.

Gelling Agent : Pluronic F - 127, 20.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4506	0.7848	1.3223	2.0572	2.8331	3.2843

$Y = 0.1147 \pm 6.4801\ x$

$r^2 = 0.9954$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0	0	0	0	0	0
1.75	0	0	0	0	0	0
2.75	0	0	0	0	0	0
3.75	0	0	0	0	0	0
4.75	0	0	0	0	0	0
5.75	0	0	0	0	0	0
6.75	0	0	0	0	0	0
Steady-state slope (mcg/hr)	-		-		-	
Lag time (hr)	-		-		-	
Steady-state flux (mcg/hr. cm^2)	-		-		-	
r^2	-		-		-	

* PAR = Peak Area Ratio

Gelling Agent : Carbopol - 940, 1.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4870	0.9469	1.8720	2.8230	3.7870	4.6439

$Y = 0.0217 + 9.3094 x$

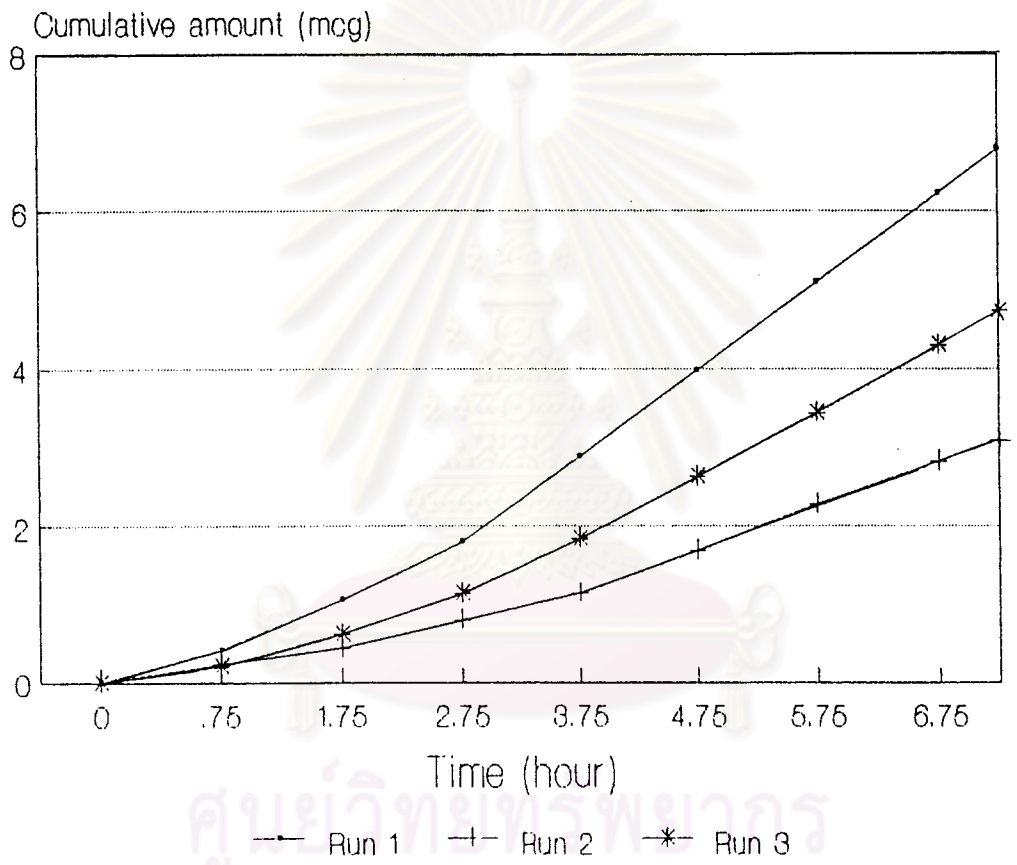
$r^2 = 0.9998$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.6751	0.4029	0.3892	0.2236	0.3266	0.1955
1.75	1.0781	0.6515	0.3789	0.2173	0.6738	0.4172
2.75	1.2302	0.7450	0.6027	0.3532	0.8377	0.5221
3.75	1.7512	1.0665	0.5841	0.3419	1.1117	0.6979
4.75	1.8007	1.0969	0.9326	0.5535	1.2548	0.7891
5.75	1.8460	1.1250	0.9910	0.5892	1.2801	0.8058
6.75	1.8573	1.1319	0.8957	0.5315	1.3843	0.8725
7.25	0.9495	0.5723	0.5118	0.2977	0.8125	0.5060
Steady-state slope (mcg/hr)	1.1228		0.5628		0.8689	
Lag time (hr)	1.21		1.73		1.76	
Steady-state flux (mcg/hr. cm^2)	0.8019		0.3654		0.5642	
r^2	0.9999		0.9995		0.9983	

* PAR = Peak Area Ratio $\bar{J}ss = 0.5772 \pm 0.2185$ % CV = 37.86

Piroxicam flux from carbopol-940 gel base through pig skin.



Gelling Agent : Hydroxypropyl Methylcellulose, 3.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.6051	0.9535	1.8974	2.9016	3.9213	4.7695

$Y = 0.0598 + 9.4772\ x$

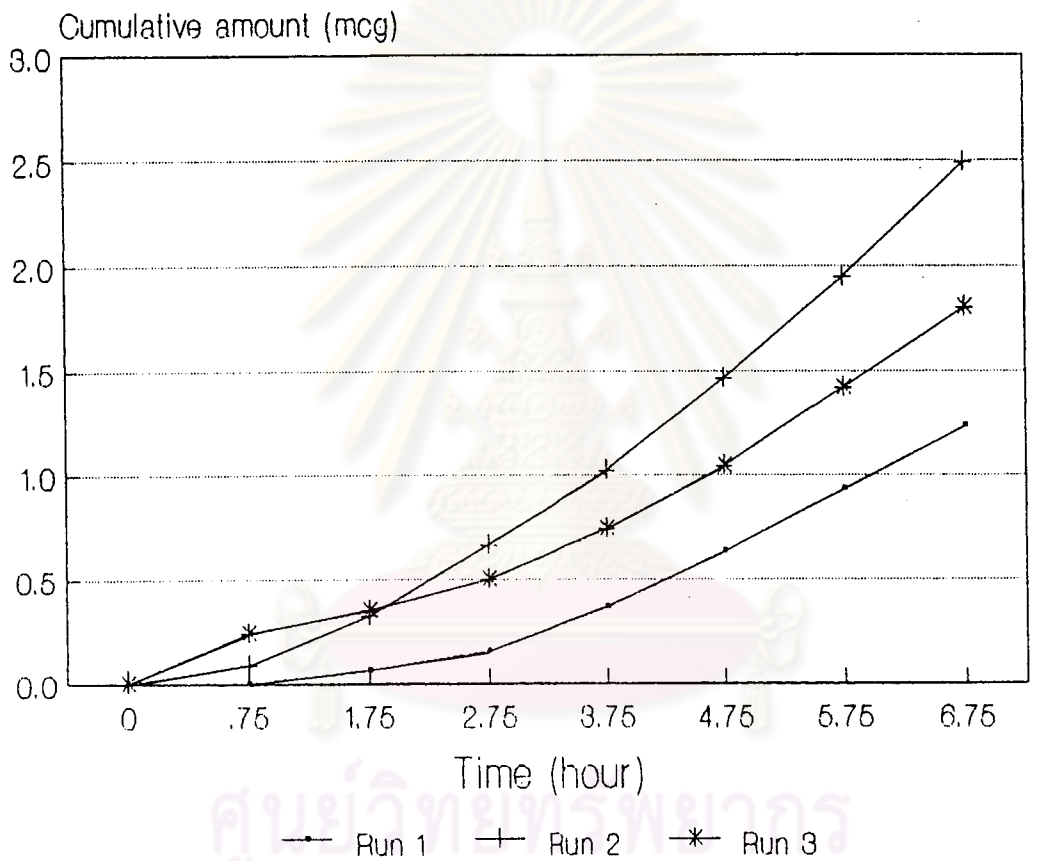
$r^2 = 0.9987$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	-	-	0.2066	0.0877	0.4396	0.2390
1.75	0.1583	0.0597	0.4563	0.2366	0.2340	0.1097
2.75	0.2147	0.0936	0.6277	0.3390	0.2960	0.1484
3.75	0.4093	0.2118	0.6534	0.3543	0.4486	0.2444
4.75	0.4998	0.2663	0.8068	0.4460	0.5334	0.2980
5.75	0.5513	0.2979	0.8678	0.4822	0.6593	0.3767
6.75	0.5560	0.3008	0.9759	0.5473	0.6718	0.3850
Steady-state slope (mcg/hr)	0.2893		0.4909		0.3556	
Lag time (hr)	2.52		1.72		1.74	
Steady-state flux (mcg/hr. cm^2)	0.1878		0.3187		0.2309	
r^2	0.9992		0.9978		0.9966	

* PAR = Peak Area Ratio $\bar{J}ss = 0.2458 \pm 0.0667$ % CV = 27.14

Piroxicam flux form HPMC gel base through pig skin.



Gelling Agent : Hydroxyethyl Cellulose, 2.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4179	0.7573	1.3625	2.1890	3.0510	3.6738

$Y = - 0.0021 + 7.3961 x$

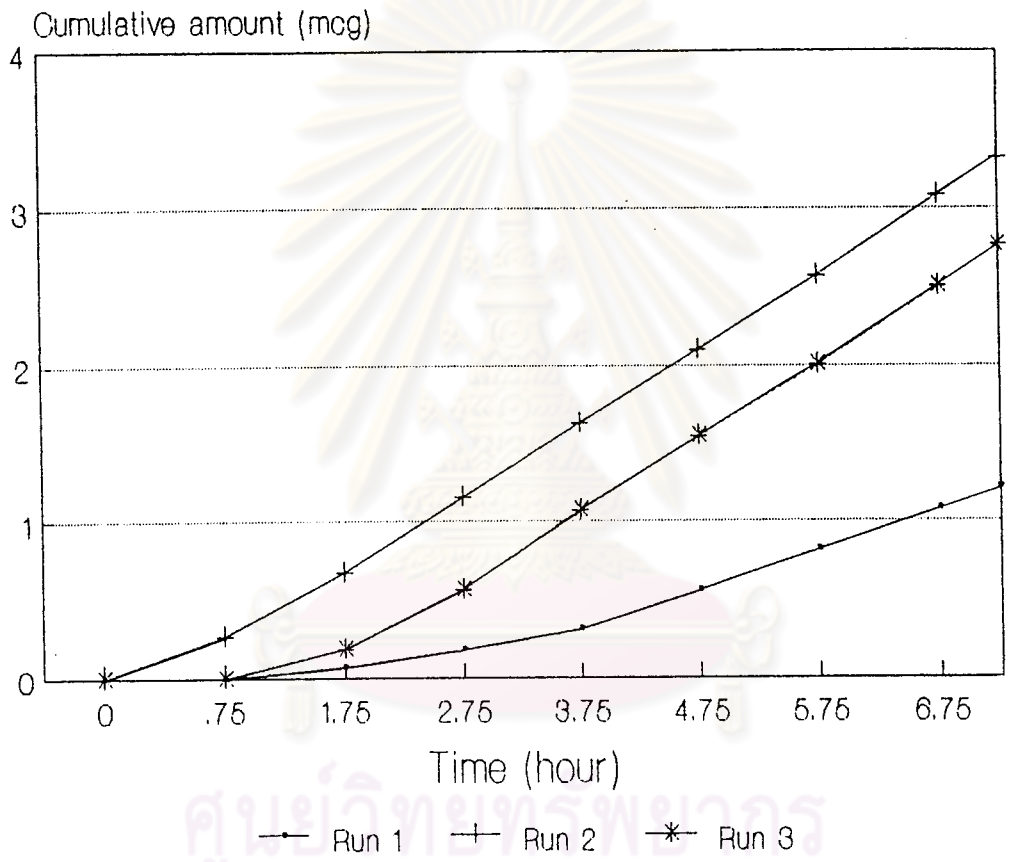
$r^2 = 0.9968$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	-	-	0.3442	0.2686	-	-
1.75	0.0844	0.0697	0.5204	0.4052	0.2396	0.1861
2.75	0.1298	0.1061	0.6176	0.4810	0.4818	0.3721
3.75	0.1602	0.1305	0.6023	0.4690	0.6589	0.5087
4.75	0.3017	0.2450	0.6148	0.4787	0.6133	0.4734
5.75	0.3285	0.2664	0.6017	0.4684	0.6025	0.4649
6.75	0.3203	0.2598	0.6579	0.5120	0.6511	0.5024
7.25	0.1624	0.1323	0.3313	0.2589	0.3442	0.2663
Steady-state slope (mcg/hr)	0.2630		0.4966		0.4930	
Lag time (hr)	2.65		0.54		1.65	
Steady-state flux (mcg/hr. cm^2)	0.1708		0.3225		0.3201	
r^2	0.9999		0.9994		0.9993	

* PAR = Peak Area Ratio $\bar{J}ss = 0.2711 \pm 0.0869$ % CV = 32.05

Piroxicam flux form HEC gel base through pig skin .



Appendix IV

Data of Piroxicam Fluxes from Carbopol-940 Gel Bases Containing Various Additives through Silastic®.

Additive : Isopropyl Alcohol, 10 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.3975	0.7027	1.7275	2.5439	3.4632	4.4608

$Y = - 0.1278 + 9.0726 x$

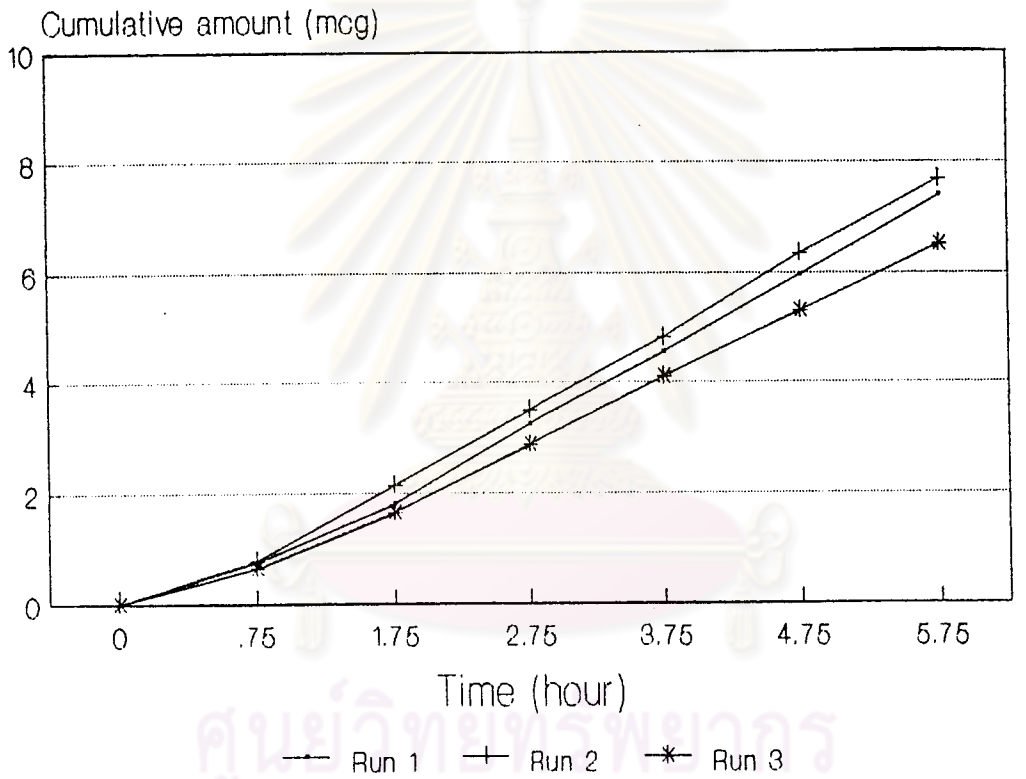
$r^2 = 0.9984$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	1.0239	0.7284	1.0594	0.7796	0.8832	0.6339
1.75	1.5833	1.0826	1.9194	1.3446	1.4956	1.0179
2.75	2.1261	1.4258	1.9444	1.3613	1.8222	1.2228
3.75	1.9344	1.3047	1.9029	1.3338	1.8020	1.2103
4.75	2.0963	1.4069	2.1852	1.5192	1.8060	1.2125
5.75	2.1501	1.4413	1.9115	1.3398	1.8332	1.2296
Steady-state slope (mcg/hr)	1.3866		1.4098		1.2170	
Lag time (hr)	0.44		0.29		0.39	
Steady-state flux (mcg/hr. cm^2)	0.9004		0.9154		0.7902	
r^2	0.9995		0.9993		0.9999	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 0.8687 \pm 0.0684 \quad$ % CV = 7.87

Piroxicam flux from carbopol-940 gel base containing 10 % isopropyl alcohol through silastic®.



Additive : Isopropyl Alcohol, 20 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.3975	0.7027	1.7275	2.5439	3.4632	4.4608

$Y = - 0.1278 + 9.0726 x$

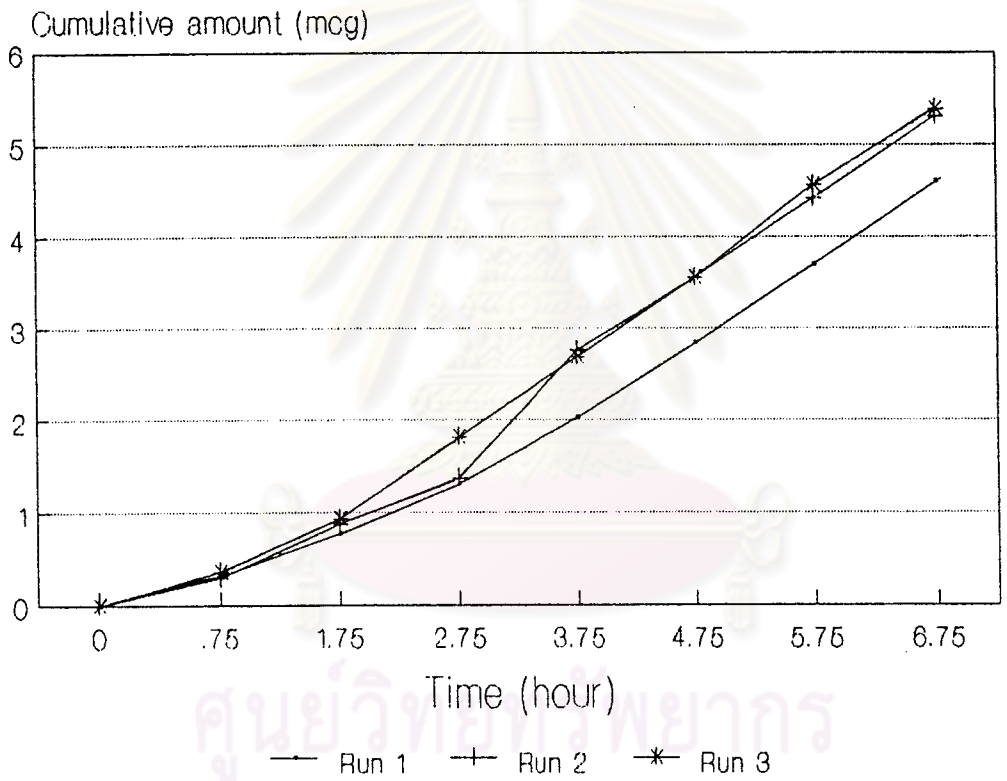
$r^2 = 0.9984$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.3638	0.3111	0.3314	0.2864	0.4155	0.3570
1.75	0.5919	0.4552	0.8178	0.5898	0.7405	0.5704
2.75	0.7218	0.5373	0.6728	0.4992	1.2218	0.8868
3.75	1.0089	0.7192	2.0875	1.3822	1.1942	0.8684
4.75	1.1719	0.8220	1.1642	0.8060	1.2129	0.8809
5.75	1.2305	0.8593	1.2615	0.8665	1.3886	0.9959
6.75	1.2957	0.9006	1.2713	0.8728	1.1156	0.8165
Steady-state slope (mcg/hr)	0.8605		0.8502		0.9000	
Lag time (hr)	1.42		0.53		0.75	
Steady-state flux (mcg/hr. cm^2)	0.5588		0.5521		0.5844	
r^2	0.9996		0.9996		0.9993	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 0.5651 \pm 0.0170 \quad$ % CV = 3.02

Piroxicam flux from carbopol-940 gel base containing 20 % isopropyl alcohol through silastic®.



Additive : Propylene Glycol, 5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4584	0.9637	1.7618	2.5630	3.6803	4.2493

$Y = 0.0640 + 8.5757 x$

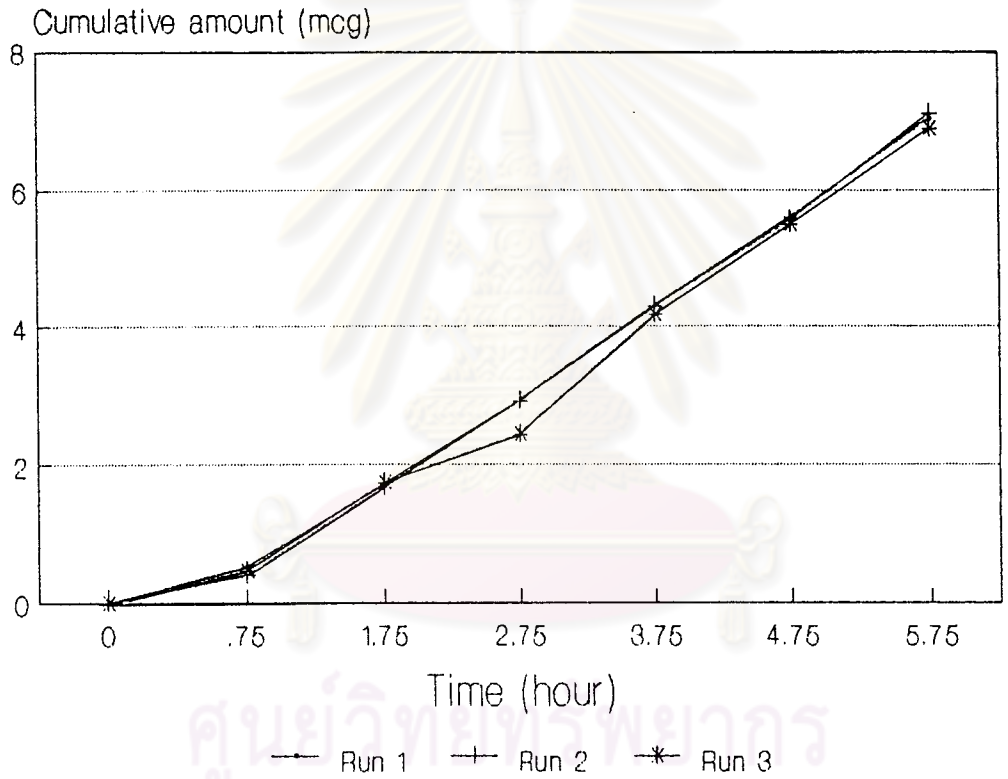
$r^2 = 0.9952$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.8494	0.5258	0.6775	0.4047	0.7356	0.4667
1.75	1.8467	1.1933	1.9844	1.2673	1.8913	1.2701
2.75	1.8784	1.2146	1.9500	1.2446	1.7968	1.2039
3.75	2.1185	1.3753	2.1669	1.3878	1.8325	1.2290
4.75	2.0064	1.3001	1.9668	1.2560	1.9804	1.3321
5.75	2.1671	1.4074	2.3885	1.5339	2.0409	1.3738
Steady-state slope (mcg/hr)	1.3548		1.3789		1.4637	
Lag time (hr)	0.58		0.65		1.01	
Steady-state flux (mcg/hr. cm^2)	0.8798		0.8954		0.9504	
r^2	0.9998		0.9986		0.9962	

* PAR = Peak Area Ratio $\bar{J}ss = 0.9085 \pm 0.0371$ % CV = 4.08

Piroxicam flux from carbopol-940 gel base containing 5 % propylene glycol through silastic®.



Additive : Propylene Glycol, 10 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4584	0.9637	1.7618	2.5630	3.6803	4.2493

$Y = 0.0640 + 8.5757 x$

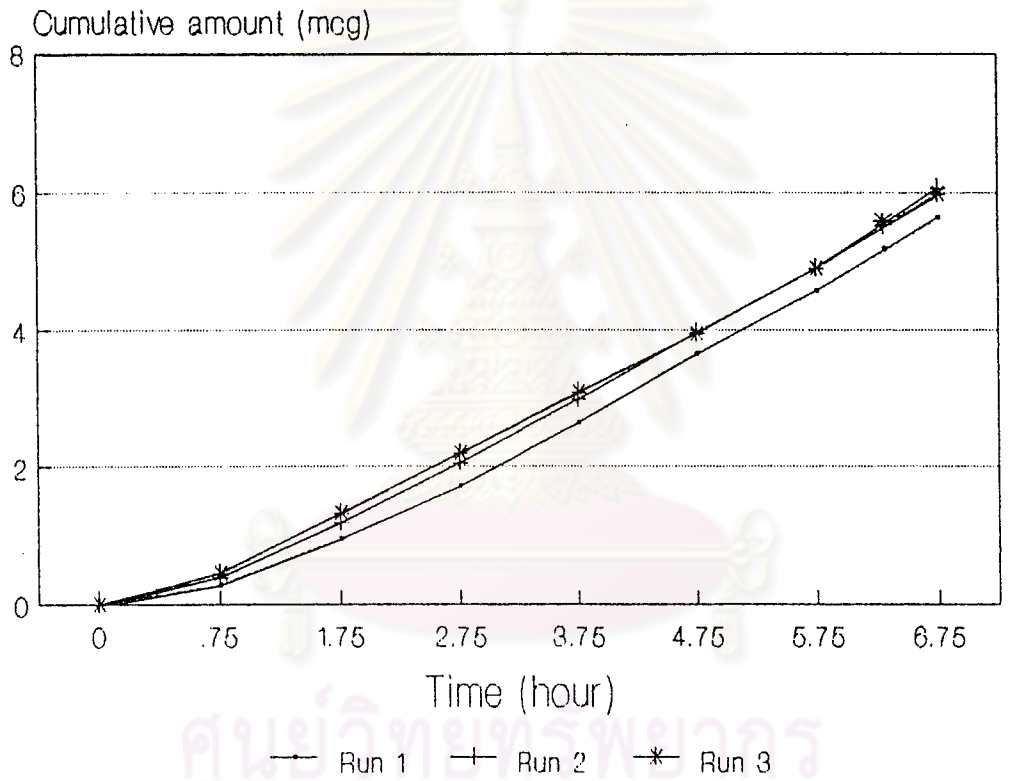
$r^2 = 0.9952$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.4744	0.2744	0.6437	0.3826	0.7365	0.4461
1.75	1.0700	0.6733	1.2709	0.7964	1.3681	0.8654
2.75	1.1875	0.7519	1.3898	0.8750	1.3756	0.8700
3.75	1.4590	0.9339	1.4548	0.9180	1.4366	0.9104
4.75	1.5742	1.0108	1.5527	0.9826	1.3354	0.8432
5.75	1.4490	0.9270	1.5124	0.9560	1.5249	0.9696
6.25	0.9481	0.5918	1.0304	0.6379	1.0398	0.6475
6.75	0.7584	0.4649	0.8210	0.4998	0.7077	0.4268
Steady-state slope (mcg/hr)	0.9118		0.9625		0.9474	
Lag time (hr)	0.89		0.63		0.42	
Steady-state flux (mcg/hr. cm^2)	0.5920		0.6250		0.6152	
r^2	0.9999		0.9999		0.9994	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 0.6107 \pm 0.0169 \quad$ % CV = 2.78

Piroxicam flux from carbopol-940 gel base containing 10 % propylene glycol through silastic®.



Additive : Tween 20, 0.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0600	0.1200	0.2400	0.3000	0.3600	0.4800
Peak Area Ratio	0.3325	0.6758	1.3662	1.6284	2.0296	2.7283

$Y = - 0.0130 + 5.6657 x$

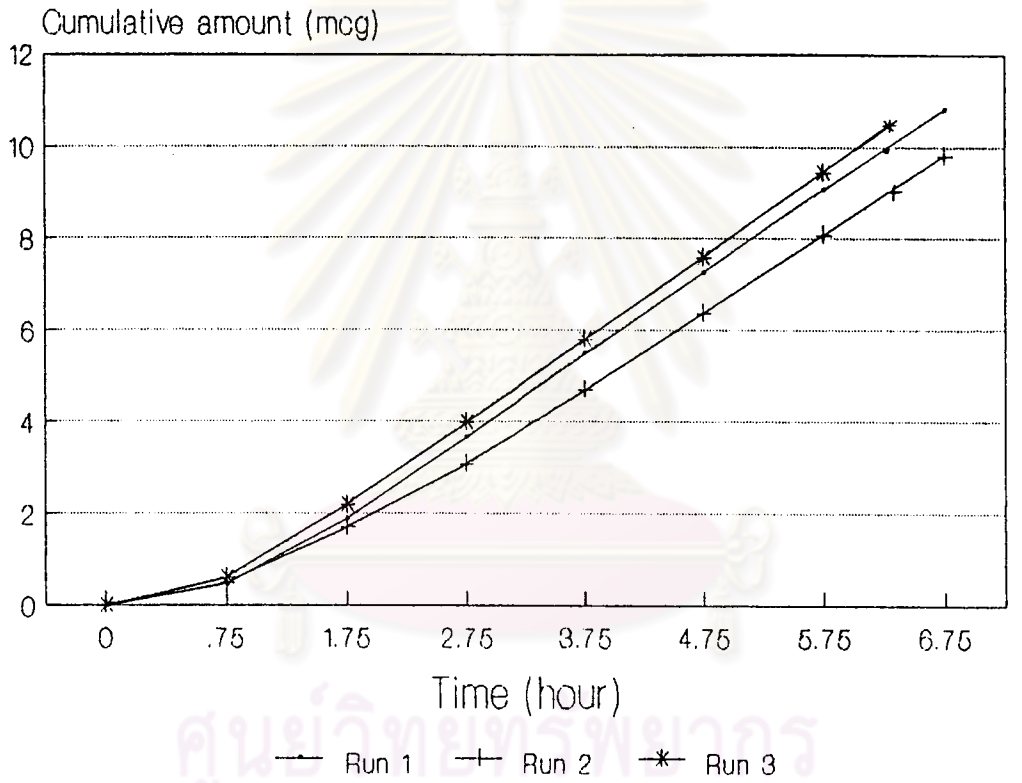
$r^2 = 0.9989$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.4312	0.4500	0.4662	0.4788	0.5622	0.6049
1.75	1.4082	1.4396	1.2155	1.2271	1.5005	1.5919
2.75	1.7363	1.7719	1.3445	1.3561	1.6825	1.7832
3.75	1.7865	1.8230	1.6104	1.6261	1.7110	1.8136
4.75	1.7511	1.7874	1.6893	1.7003	1.7054	1.8077
5.75	1.7557	1.7920	1.6769	1.6878	1.7164	1.8190
6.25	0.8289	0.8530	0.8689	0.8807	0.9624	1.0257
6.75	0.8542	0.8782	0.8347	0.8467	-	-
Steady-state slope (mcg/hr)	1.7830		1.7054		1.8366	
Lag time (hr)	0.68		1.01		0.59	
Steady-state flux (mcg/hr. cm^2)	1.1578		1.1074		1.1926	
r^2	0.9999		0.9999		0.9997	

* PAR = Peak Area Ratio $\bar{J}ss = 1.1526 \pm 0.0428$ % CV = 3.72

Piroxicam flux from carbopol-940 gel base containing 0.5 % Tween 20 through silastic®.



Additive : Tween 20, 1.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0600	0.1200	0.2400	0.3000	0.3600	0.4800
Peak Area Ratio	0.3325	0.6758	1.3662	1.6284	2.0296	2.7283

$Y = -0.0130 + 5.6657 x$

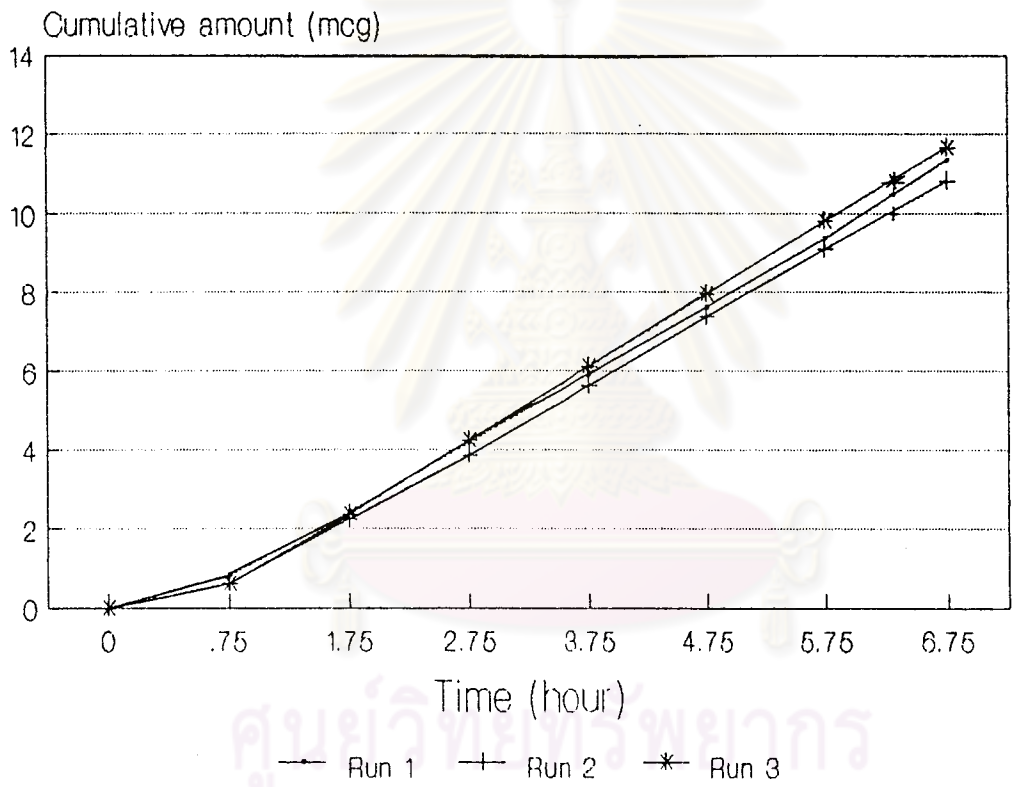
$r^2 = 0.9989$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.8162	0.8398	0.6070	0.6192	0.5653	0.6085
1.75	1.5538	1.5871	1.6201	1.6312	1.6458	1.7451
2.75	1.7145	1.7501	1.6032	1.6142	1.7843	1.8905
3.75	1.6960	1.7312	1.7475	1.7586	1.7673	1.8726
4.75	1.7021	1.7375	1.7486	1.7597	1.7276	1.8309
5.75	1.7012	1.7364	1.7149	1.7263	1.7423	1.8464
6.25	0.9824	1.0085	0.8029	0.8150	0.8671	0.9256
6.75	0.9043	0.9293	0.8832	0.8954	0.8728	0.9315
Steady-state slope (mcg/hr)	1.8410		1.7117		1.8511	
Lag time (hr)	0.61		0.44		0.46	
Steady-state flux (mcg/hr. cm^2)	1.1955		1.1115		1.2020	
r^2	0.9990		0.9998		0.9999	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 1.1697 \pm 0.0505 \quad$ % CV = 4.32

Piroxicam flux from carbopol-940 gel base containing 1.0 % Tween 20 through silastic®.



Additive : Brij 30, 0.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0600	0.1200	0.2400	0.3000	0.3600	0.4800
Peak Area Ratio	0.2702	0.5355	1.0774	1.2618	1.5853	2.1019

$Y = 0.0101 + 4.3405 x$

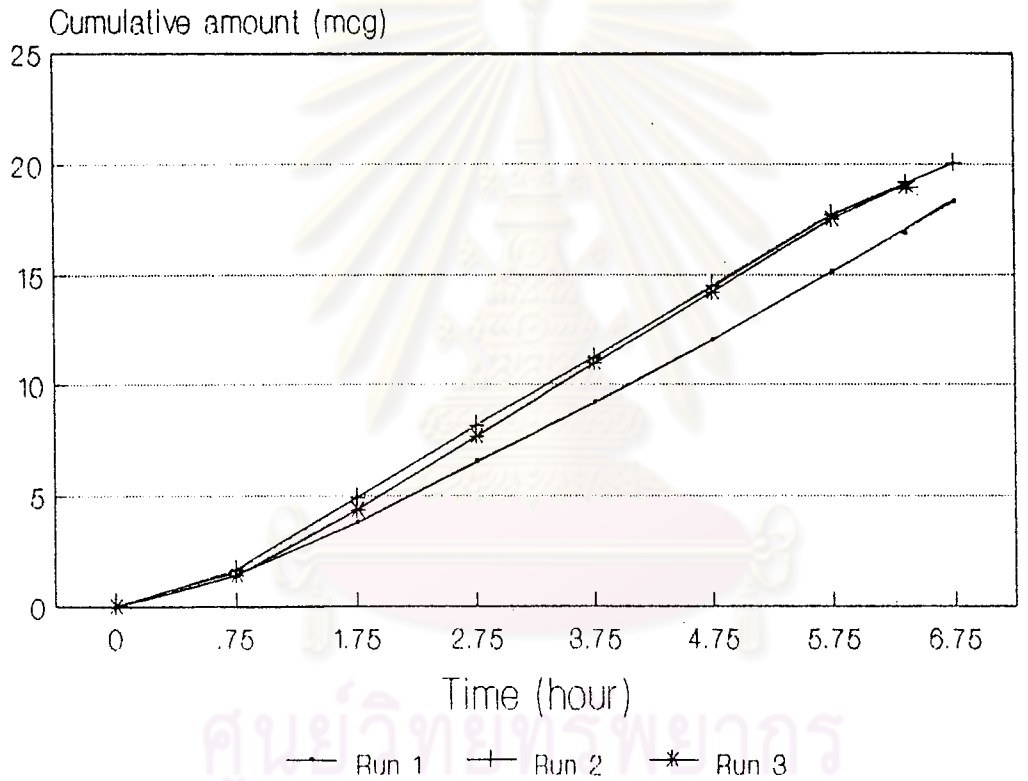
$r^2 = 0.9985$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	1.0732	1.4057	1.2747	1.6488	1.0183	1.3845
1.75	1.7873	2.3500	2.5026	3.2500	2.1918	2.9955
2.75	2.1194	2.7891	2.5146	3.2658	2.4019	3.2840
3.75	1.9867	2.6140	2.3215	3.0140	2.4056	3.2893
4.75	2.1714	2.8579	2.5513	3.3134	2.3761	3.2488
5.75	2.3543	3.1002	2.4861	3.2285	2.4185	3.3066
6.25	1.2210	1.6015	1.2550	1.6233	1.4272	1.6616
6.75	1.1809	1.5481	1.3142	1.7003	-	-
Steady-state slope (mcg/hr)	2.9494		2.9752		3.2845	
Lag time (hr)	0.60		-0.04		0.42	
Steady-state flux (mcg/hr. cm^2)	1.9152		1.9320		2.1328	
r^2	0.9987		0.9953		0.9999	

* PAR = Peak Area Ratio $\bar{J}ss = 1.9933 \pm 0.1211$ % CV = 6.07

Piroxicam flux from carbopol-940 gel base containing 0.5 % Brij 30 through silastic®.



Additive : Brij 30, 1.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0600	0.1200	0.2400	0.3000	0.3600	0.4800
Peak Area Ratio	0.3325	0.6758	1.3662	1.6284	2.0296	2.7283

$Y = - 0.0130 + 5.6657 x$

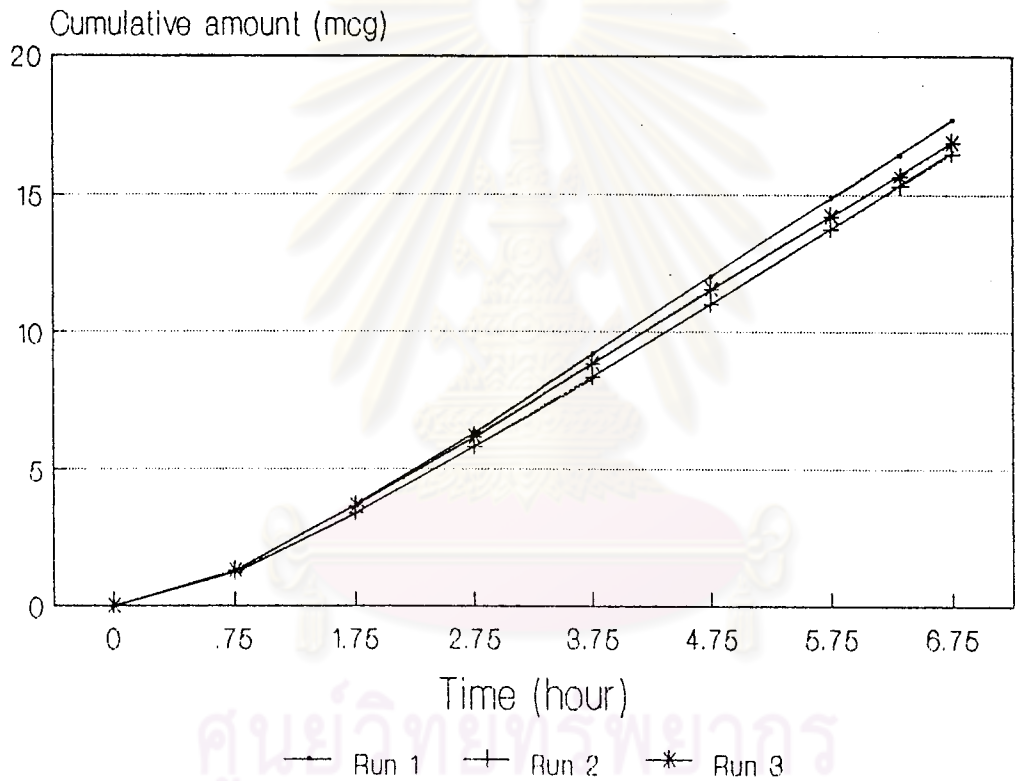
$r^2 = 0.9989$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	1.2594	1.2892	1.1743	1.1863	1.1823	1.2576
1.75	2.3474	2.3913	2.1611	2.1717	2.2470	2.3774
2.75	2.6113	2.6588	2.4597	2.4700	2.3918	2.5294
3.75	2.7974	2.8470	2.5196	2.5300	2.5395	2.6850
4.75	2.7981	2.8482	2.6591	2.6692	2.5779	2.7255
5.75	2.7639	2.8132	2.6929	2.7032	2.4977	2.6408
6.25	1.3486	1.3793	1.5433	1.5548	1.2357	1.3136
6.75	1.3904	1.4218	1.1440	1.1558	1.2548	1.3338
Steady-state slope (mcg/hr)	2.8170		2.7229		2.6662	
Lag time (hr)	0.48		0.69		0.42	
Steady-state flux (mcg/hr. cm^2)	1.8292		1.7681		1.7313	
r^2	0.9999		0.9993		0.9999	

* PAR = Peak Area Ratio $\bar{J}ss = 1.7762 \pm 0.0494$ % CV = 2.78

Piroxicam flux from carbopol-940 gel base containing 1.0 % Brij 30 through silastic®.



Appendix V

Data of Piroxicam Fluxes from Carbopol-940 Gel Bases Containing Various Additives through Pig Skin.

Additive : Isopropyl Alcohol, 10 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.3975	0.7027	1.7275	2.5439	3.4632	4.4608

$Y = -0.1278 + 9.0726 x$

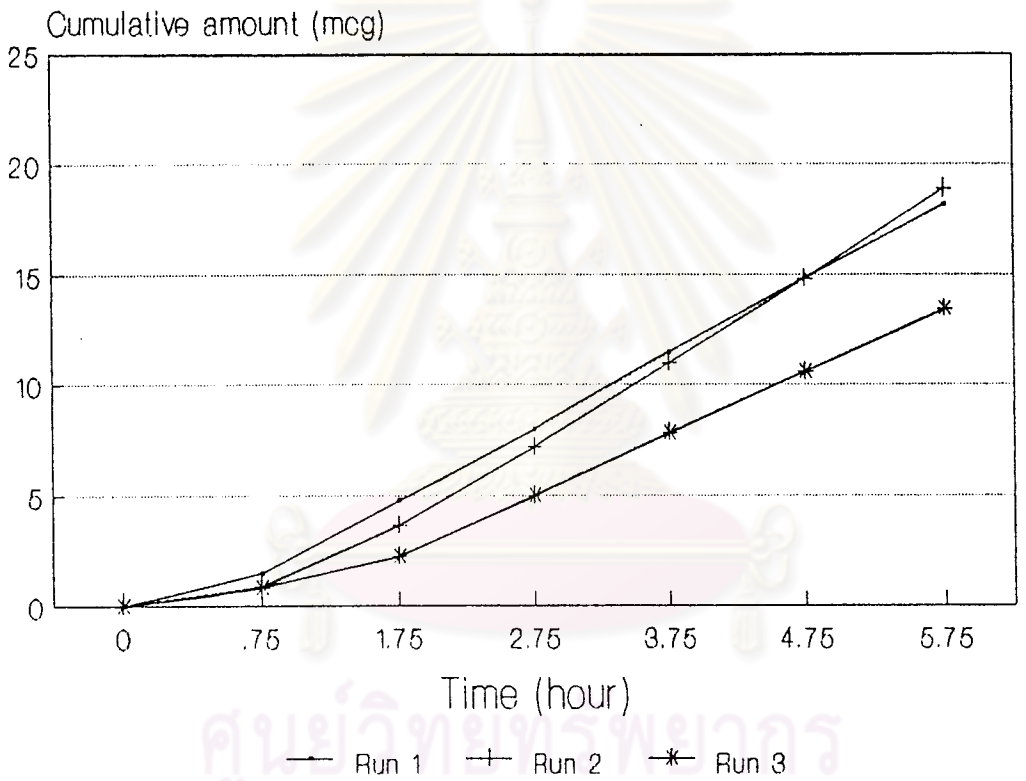
$r^2 = 0.9984$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	2.1645	1.4303	1.2104	0.8791	1.2065	0.8370
1.75	5.1648	3.3020	4.0290	2.7309	2.1079	1.4020
2.75	5.0637	3.2386	5.2664	3.5438	4.2838	2.7665
3.75	5.4111	3.4554	5.6804	3.8156	4.3116	2.7841
4.75	5.3787	3.4350	5.6826	3.8168	4.3284	2.7949
5.75	5.1711	3.3054	6.0828	4.0796	4.4048	2.8427
Steady-state slope (mcg/hr)	3.4022		3.8953		2.8060	
Lag time (hr)	0.40		0.93		0.97	
Steady-state flux (mcg/hr. cm^2)	2.2092		2.5294		1.8221	
r^2	0.9999		0.9997		0.9999	

* PAR = Peak Area Ratio $\bar{J}ss = 2.1869 \pm 0.3542$ % CV = 16.20

Piroxicam flux from carbopol-940 gel base containing 10 % isopropyl alcohol through pig skin.



Additive : Isopropyl Alcohol, 20 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4073	0.9706	1.8046	2.7469	4.2858	5.2964

$Y = -0.2307 + 10.9004\ x$

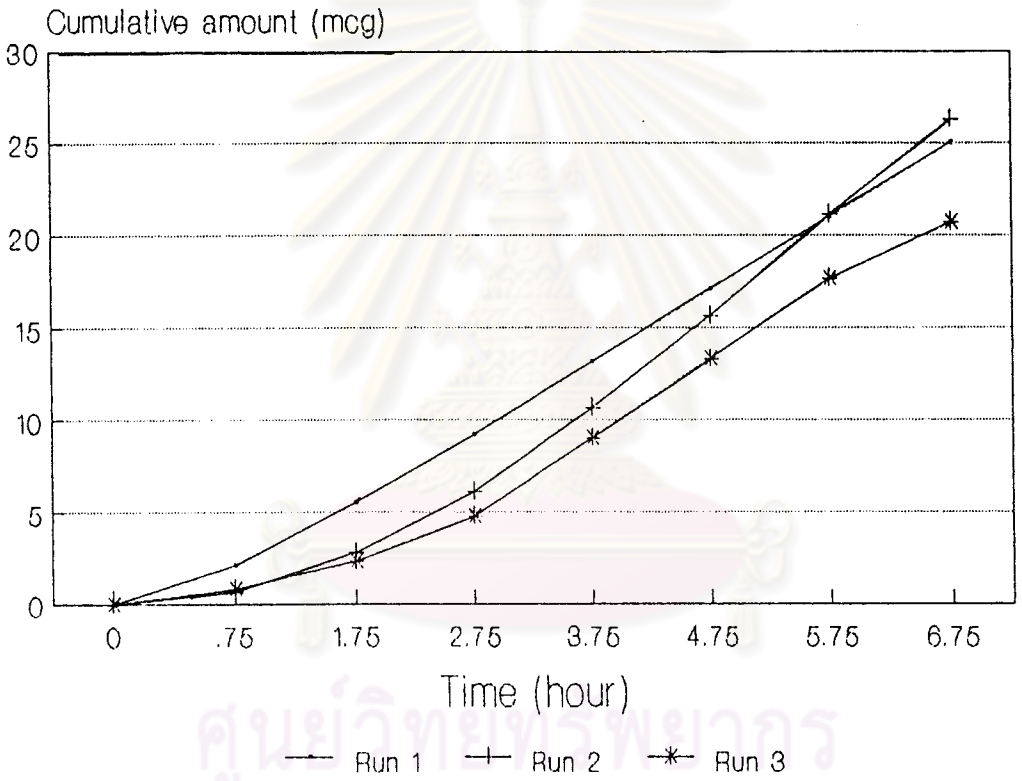
$r^2 = 0.9913$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	3.7990	2.0925	0.9053	0.6210	1.3361	0.8176
1.75	6.3286	3.4056	3.6703	2.1331	2.6965	1.5278
2.75	6.8623	3.6830	5.9472	3.3781	4.4517	2.4444
3.75	7.4188	3.9722	8.0799	4.5439	7.9106	4.2499
4.75	7.3653	3.9439	9.4497	5.2931	8.0279	4.3107
5.75	7.3260	3.9235	9.1700	5.1399	8.0472	4.3210
6.75	7.3451	3.9337	9.1401	5.1238	5.6342	3.0612
Steady-state slope (mcg/hr)	3.9327		5.1810		3.9400	
Lag time (hr)	0.40		1.68		1.39	
Steady-state flux (mcg/hr. cm^2)	2.5537		3.3643		2.5584	
r^2	0.9999		0.9999		0.9940	

* PAR = Peak Area Ratio $\quad \overline{Jss} = 2.8255 \pm 0.4666 \quad$ % CV = 16.52

Piroxicam flux from carbopol-940 gel base containing 20 % isopropyl alcohol through pig skin.



Additive : Propylene Glycol, 5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4584	0.9637	1.7618	2.5630	3.6803	4.2493

$Y = -0.0640 + 8.5757 x$

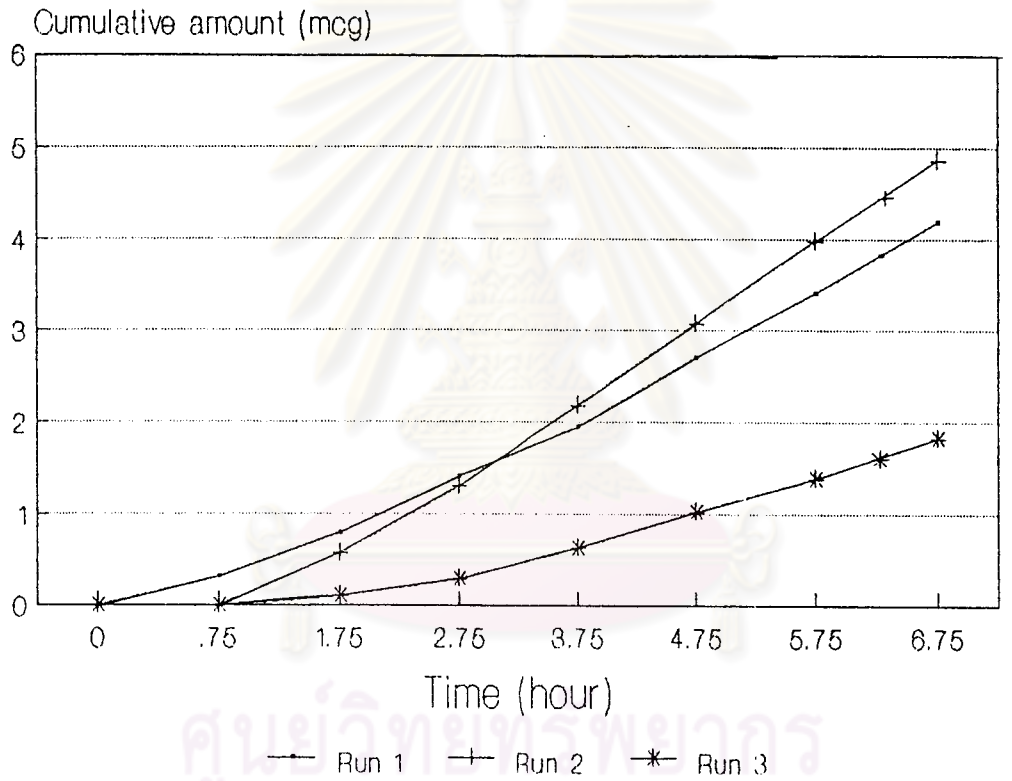
$r^2 = 0.9952$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.5254	0.3088	-	-	-	-
1.75	0.7867	0.4839	0.9254	0.5683	0.2074	0.0995
2.75	0.9820	0.6142	1.1690	0.7290	0.3281	0.1836
3.75	0.8592	0.5321	1.4032	0.8841	0.5624	0.3463
4.75	1.2011	0.7611	1.4073	0.8864	0.6214	0.3874
5.75	1.1185	0.7060	1.4526	0.9186	0.5921	0.3671
6.25	0.7208	0.4397	0.7238	0.4352	0.3584	0.2044
6.75	0.5876	0.3501	0.7201	0.4330	0.4035	0.2360
Steady-state slope (mcg/hr)	0.7544		0.8943		0.4000	
Lag time (hr)	1.19		1.31		2.24	
Steady-state flux (mcg/hr. cm^2)	0.4899		0.5807		0.2597	
r^2	0.9983		0.9997		0.9965	

* PAR = Peak Area Ratio $\bar{J}ss = 0.4434 \pm 0.1655$ % CV = 37.32

Piroxicam flux from carbopol-940 gel base containing 5 % propylene glycol through pig skin.



Additive : Propylene Glycol, 10 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4285	0.8738	1.7714	2.4120	3.2156	4.2015

$Y = -0.0434 + 8.1564 x$

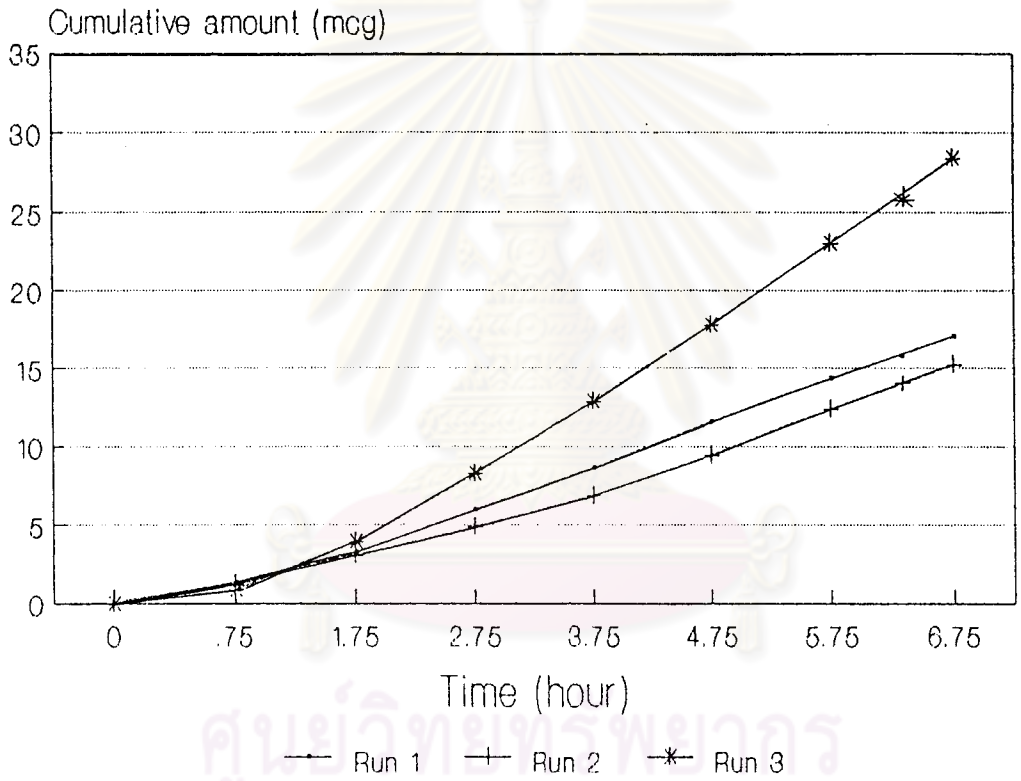
$r^2 = 0.9970$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	1.9265	1.3254	1.8214	1.2339	1.2494	0.8410
1.75	2.8143	1.9499	2.6280	1.7936	4.4829	3.0971
2.75	3.8440	2.6748	2.7098	1.8502	6.2630	4.3386
3.75	3.8565	2.6834	2.9066	1.9867	6.6161	4.5850
4.75	4.1351	2.8792	3.7878	2.5985	7.1466	4.9554
5.75	3.9979	2.7828	4.1784	2.8696	7.5099	5.2086
6.25	2.0531	1.4143	2.4811	1.6918	3.7853	2.6106
6.75	1.9724	1.3575	1.7428	1.1795	3.9502	2.7255
Steady-state slope (mcg/hr)	2.8117		2.9143		5.2607	
Lag time (hr)	0.67		1.50		1.37	
Steady-state flux (mcg/hr. cm^2)	1.8258		1.8924		3.4160	
r^2	0.9999		0.9976		0.9999	

* PAR = Peak Area Ratio $\bar{J}ss = 2.3781 \pm 0.8995$ % CV = 37.82

Piroxicam flux from carbopol-940 gel base containing 10 % propylene glycol through pig skin.



Additive : Tween 20, 0.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.4612	0.8057	1.6391	2.4324	3.1510	3.9806

$Y = 0.0562 + 7.8276\ x$

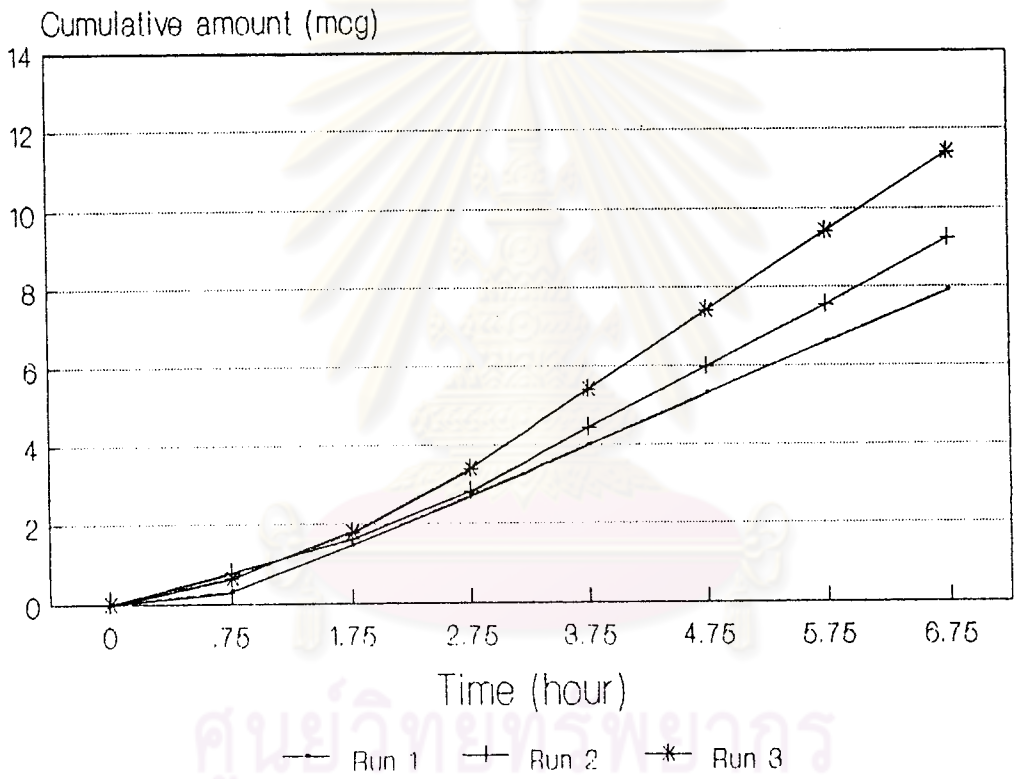
$r^2 = 0.9996$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.4865	0.3157	1.1540	0.7935	0.9136	0.6526
1.75	1.6272	1.1520	1.2098	0.8343	1.5657	1.1491
2.75	1.7524	1.2438	1.7107	1.1965	2.1365	1.5842
3.75	1.8018	1.2800	2.2748	1.6040	2.6949	2.0091
4.75	1.8356	1.3047	2.1953	1.5469	2.7020	2.0145
5.75	1.8463	1.3127	2.2335	1.5746	2.7133	2.0228
6.75	1.8379	1.3064	2.3716	1.6742	2.6692	1.9894
Steady-state slope (mcg/hr)	1.3084		1.5962		2.0103	
Lag time (hr)	1.70		0.99		1.06	
Steady-state flux (mcg/hr. cm^2)	0.8496		1.0365		1.3054	
r^2	0.9999		0.9997		0.9999	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 1.0638 \pm 0.2291 \quad$ % CV = 21.54

Piroxicam flux from carbopol-940 gel base containing 0.5 % Tween 20 through pig skin.



Additive : Tween 20, 1.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.3141	0.7904	1.6985	2.6021	3.4647	4.2774

$Y = -0.0906 + 8.8326\ x$

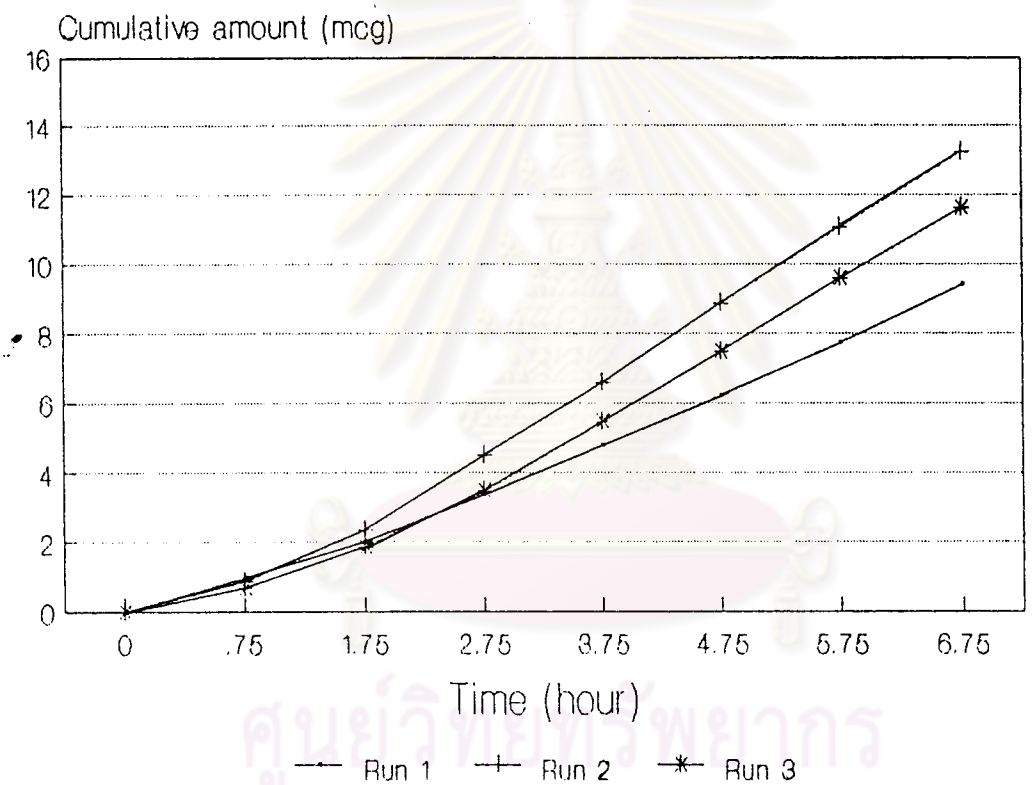
$r^2 = 0.9994$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	1.3834	0.9580	1.2347	0.8490	0.9271	0.6866
1.75	1.5458	1.0636	2.2531	1.5016	1.6368	1.1658
2.75	1.9767	1.3432	3.2646	2.1502	2.2913	1.6074
3.75	2.1022	1.4247	3.1762	2.0931	2.8529	1.9859
4.75	2.0973	1.4218	3.4549	2.2719	2.9311	2.0389
5.75	2.2498	1.5211	3.2985	2.1717	3.0139	2.0949
6.75	2.4991	1.6830	3.3253	2.1887	2.9431	2.0473
Steady-state slope (mcg/hr)	1.5399		2.1894		2.0638	
Lag time (hr)	0.68		0.71		1.11	
Steady-state flux (mcg/hr. cm^2)	0.9999		1.4217		1.3401	
r^2	0.9985		0.9999		0.9999	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 1.2539 \pm 0.2237 \quad$ % CV = 17.84

Piroxicam flux from carbopol-940 gel base containing 1.0 % Tween 20 through pig skin.



Additive : Brij 30, 0.5 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.3436	0.7354	1.5974	2.4477	3.3155	4.3224

$Y = - 0.1408 + 8.7785 x$

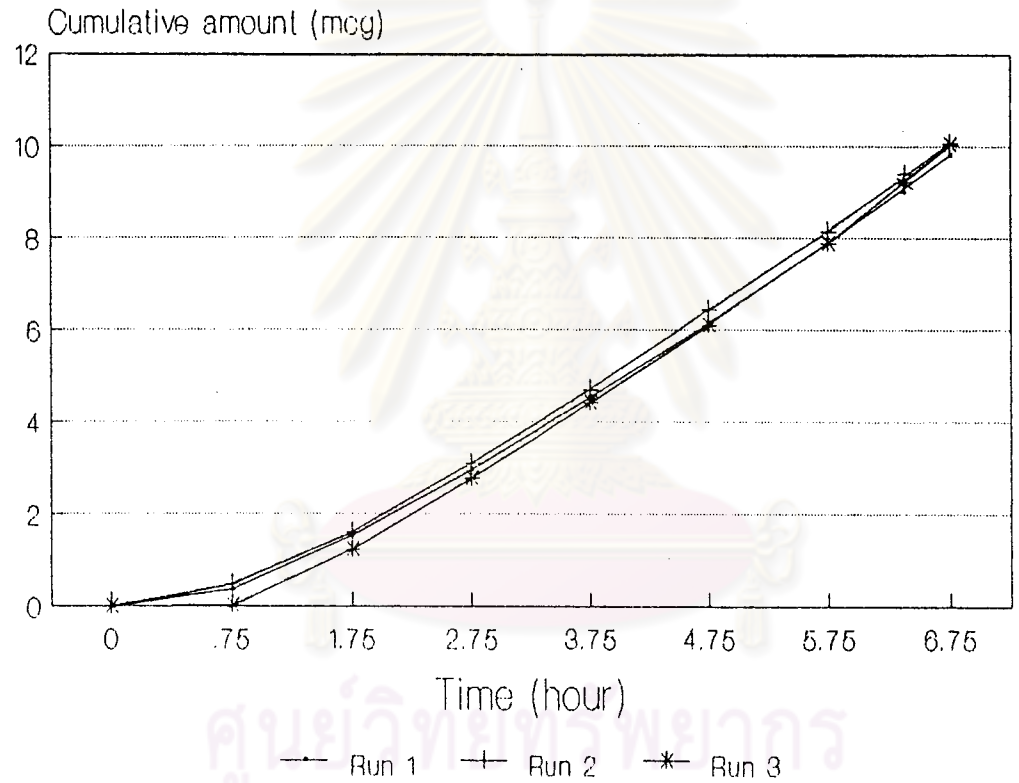
$r^2 = 0.9989$

Diffusion Run Data :

Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	0.4262	0.3656	0.5975	0.4785	0.3739	0.0227
1.75	1.6802	1.1739	1.5788	1.1147	1.6982	1.2025
2.75	2.0473	1.4105	2.1748	1.5010	2.2045	1.5337
3.75	2.3074	1.5786	2.3556	1.6182	2.4018	1.6623
4.75	2.3665	1.6165	2.5383	1.7366	2.4676	1.6795
5.75	2.5677	1.7461	2.4897	1.7047	2.5906	1.7857
6.25	1.3756	0.9775	1.3680	0.9781	1.7141	1.2129
6.75	1.3219	0.9430	1.2768	0.9189	1.3078	0.9471
Steady-state slope (mcg/hr)	1.8338		1.8032		1.9903	
Lag time (hr)	1.41		1.19		1.71	
Steady-state flux (mcg/hr. cm^2)	1.1908		1.1709		1.2924	
r^2	0.9993		0.9991		0.9965	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 1.2180 \pm 0.0652 \quad$ % CV = 5.35

Piroxicam flux from carbopol-940 gel base containing 0.5 % Brij 30 through pig skin.



Additive : Brij 30, 1.0 % W/W.

Calibration Curve Data :

Concentration (mcg/ml)	0.0500	0.1000	0.2000	0.3000	0.4000	0.5000
Peak Area Ratio	0.5145	0.8656	1.7508	2.6674	3.5871	4.3900

$Y = 0.0302 + 8.7706 x$

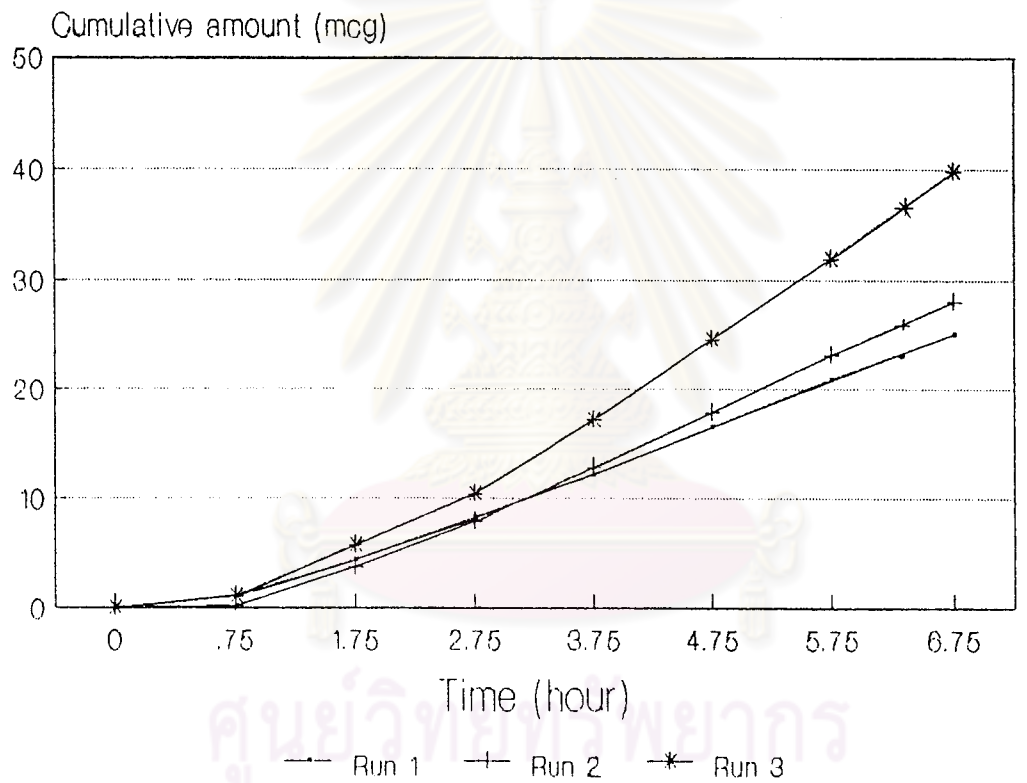
$r^2 = 0.9993$

Diffusion Run Data :

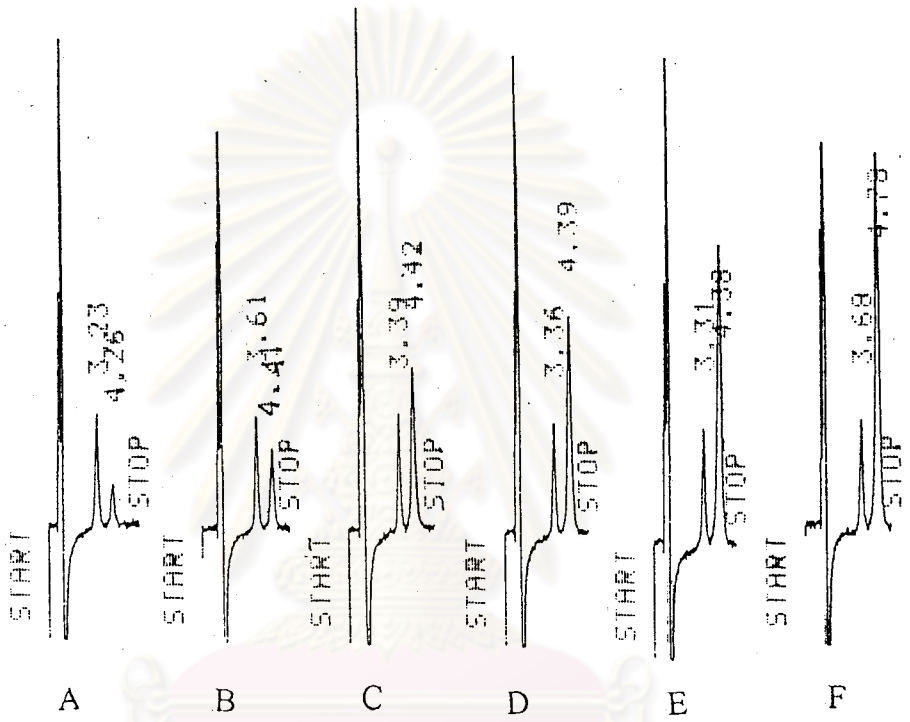
Time (hours)	Run I		Run II		Run III	
	PAR*	Amount (mcg)	PAR*	Amount (mcg)	PAR*	Amount (mcg)
0.75	1.6028	1.0148	1.6976	1.1330	1.6118	1.0259
1.75	5.2239	3.3518	5.2811	3.5682	7.1991	4.6510
2.75	5.9717	3.8341	6.1346	4.1482	7.2172	4.6624
3.75	6.0226	3.8669	7.2336	4.8949	10.5186	6.8047
4.75	6.9256	4.4499	7.4711	5.0565	11.4028	7.3782
5.75	6.6786	4.2903	7.7610	5.2531	11.3896	7.3697
6.25	3.2153	2.0557	3.9601	2.6707	6.2554	4.0388
6.75	3.3055	2.1134	3.4178	2.3018	5.9351	3.8311
Steady-state slope (mcg/hr)	4.2265		5.1484		7.6304	
Lag time (hr)	0.84		1.28		1.55	
Steady-state flux (mcg/hr. cm^2)	2.7445		3.3431		4.9548	
r^2	0.9999		0.9993		0.9996	

* PAR = Peak Area Ratio $\quad \bar{J}ss = 3.6808 \pm 1.1432 \quad$ % CV = 31.06

Piroxicam flux from carbopol-940 gel base containing 1.0 % Brij 30 through pig skin.



Appendix VI



High Performance Liquid Chromatogram of Piroxicam (retention time ~ 3.3 min.) and Tenoxicam (retention time ~ 4.4 min.) at 361 nm.

Each sample contained fix concentration of 0.25 mcg/ml tenoxicam as internal standard and various concentrations of piroxicam;

A = 0.05 mcg/ml ; B = 0.10 mcg/ml

C = 0.20 mcg/ml ; D = 0.30 mcg/ml

E = 0.40 mcg/ml ; F = 0.50 mcg/ml

VITA

Miss Busaba Polpakdee was born on 8th January 1966, in Lampang, Thailand. She got Bachelor of Science in Pharmacy in 1988 from Faculty of Pharmaceutical Sciences, Chiangmai University, Chiangmai, Thailand. Following graduation, she worked as a medical representative for two years before joining the Master's Degree programme in Pharmaceutical Sciences at Chulalongkorn University in 1990.